

AMENDMENTS TO THE SPECIFICATION

At page 55, Example 4, delete the title and insert:



At pages 124-125, delete Examples 171-173 and insert:

Example 171



The procedure described in example 4 was used but substituting Fmoc-Gln(Trt) for Fmoc-Nva. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product was purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions were lyophilized to yield N-Ac-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt: R_t = 2.80 min (gradient of 10% to 30% acetonitrile in water containing 0.01% TFA over 30 min period); MS (ESI) m/e 1037 (M)⁺; Acid Anal.: 0.98 Sar; 0.94 Gly; 0.97 Val; 2.23 Ile; 0.51 Thr; 0.90 Glu; 1.16 Arg; 1.03 Pro.

Example 172



The procedure described in example 4 was used but substituting Fmoc-D-Leu for Fmoc-D-Ile and Fmoc-Gln(Trt) for Fmoc-Nva. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product was purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions were lyophilized to yield N-Ac-Sar-Gly-Val-D-Leu-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt: R_t = 2.90 min (gradient of 10% to 30% acetonitrile in water containing 0.01% TFA over 30 min period); MS (ESI) m/e 1037 (M)⁺; Acid Anal.: 1.05 Sar; 0.97 Gly; 0.99 Val; 1.30 Leu 1.11 Ile; 0.52 Thr; 0.89 Glu; 1.20 Arg; 1.04 Pro.

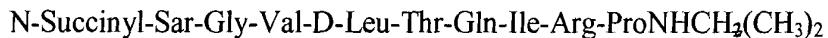
Example 173



The procedure described in example 172 was used but omitting the last coupling with acetic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product was purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions were lyophilized to yield H-Sar-Gly-Val-D-Leu-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt: R_t = 2.55 min (gradient of 10% to 30% acetonitrile in water containing 0.01% TFA over 30 min period); MS (ESI) m/e 981 (M)⁺; Acid Anal.: 1.02 Sar; 0.93 Gly; 1.02 Val; 1.05 Leu; 1.02 Ile; 0.55 Thr; 0.84 Gln; 1.31 Arg; 1.03 Pro.

At page 126, delete Example 176 and insert:

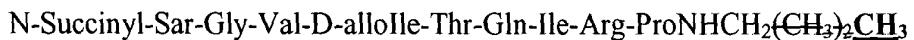
Example 176



The procedure described in example 4 was used but substituting Fmoc-D-Leu for Fmoc-D-Ile and Fmoc-Gln(Trt) for Fmoc-Nva. Following the coupling with Fmoc-Sar and protection the resin was treated with succinic anhydride/pyridine as described in example 54. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product was purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions were lyophilized to yield N-Succinyl-Sar-Gly-Val-D-Leu-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt: R_t = 2.56 min (gradient of 10% to 30% acetonitrile in water containing 0.01% TFA over 30 min period); MS (ESI) m/e 1095 (M)⁺; Acid Anal.: 0.95 Sar; 0.94 Gly; 1.02 Val; 1.02 Leu; 1.05 Ile; 0.56 Thr; 0.86 Gln; 1.00 Arg; 1.07 Pro.

At page 136, delete Examples 205 and 206 and insert:

Example 205



The procedure described in example 175 is used but substituting Fmoc-D-alloIle for Fmoc-D-Leu. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01%

TFA. The pure fractions are lyophilized to yield N-Succinyl-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃ as the trifluoroacetate salt.

Example 206

N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃

The procedure described in example 205 is used but substituting Fmoc-D-Ile for Fmoc-D-alloIle. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃ as the trifluoroacetate salt.

At pages 137, delete Example 208 and insert:

Example 208

N-Ac-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂(CH₃)₂

The procedure described in example 4 is used but substituting Fmoc-D-alloIle for Fmoc-D-Ile. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt.

At pages 137-138, delete Example 210 and insert:

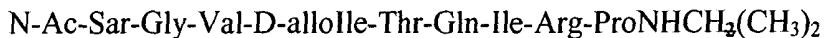
Example 210

N-Ac-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂

The procedure described in example 4 is used but substituting Fmoc-Gln(Trt) for Fmoc-Nva. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt.

At page 138, delete Example 212 and insert:

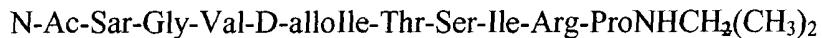
Example 212



The procedure described in example 210 is used but substituting Fmoc-D-alloIle for Fmoc-D-Ile. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt.

At page 140, delete Example 218 and insert:

Example 218



The procedure described in example 208 is used but substituting Fmoc-Ser(tBu) for Fmoc-Nva. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-alloIle-Thr-Ser-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt.

At pages 143-145, delete Examples 229-234 and insert:

Example 229



The procedure described in example 4 is used but substituting Fmoc-D-alloIle for Fmoc-D-Ile, Fmoc-Gln(Trt) for Fmoc-Nva and tetrahydro-2-furoic acid for acetic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-(2-THFcarbonyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt.

Example 230

The procedures described in examples 224, 225, 226, 227, 228, and 229 are used but substituting N-acetyl-6-aminocaproic acid (6-Ac-Aca) instead of tetrahydro-2-furoylfuroic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(6-Ac-Aca)-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(6-Ac-Aca)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(6-Ac-Aca)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(6-Ac-Aca)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂,
N-(6-Ac-Aca)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂, and
N-(6-Ac-Aca)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

Example 231

The procedures described in examples 224, 225, 226, 227, 228, and 229 are used but substituting N-acetyl-4-aminobutyric acid (4-Ac-Gaba) instead of ~~N-acetyl-6-aminocaproic acid tetrahydro-2-furoic acid~~. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(4-Ac-Gaba)-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(4-Ac-Gaba)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(4-Ac-Gaba)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(4-Ac-Gaba)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂,
N-(4-Ac-Gaba)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂, and
N-(4-Ac-Gaba)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

Example 232

The procedures described in examples 224, 225, 226, 227, 228, and 229 are used but substituting 2-furoic acid instead of tetrahydro-2-furoic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(2-Furoyl)-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(2-Furoyl)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(2-Furoyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(2-Furoyl)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂,
N-(2-Furoyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂, and
N-(2-Furoyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

Example 233

The procedures described in examples 224, 225, 226, 227, 228, and 229 are used but substituting shikimic acid instead of tetrahydro-2-furoic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(Shikimyl)-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(Shikimyl)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(Shikimyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(Shikimyl)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂,
N-(Shikimyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂, and
N-(Shikimyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

Example 234

The procedures described in examples 224, 225, 226, 227, 228, and 229 are used but substituting 2-methyl-nicotinic acid instead of tetrahydro-2-furoic acid. After cleavage of the

peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides:

N-(2-Me-Nicotinyl)-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(2-Me-Nicotinyl)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(2-Me-Nicotinyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(2-Me-Nicotinyl)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂,
N-(2-Me-Nicotinyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂, and
N-(2-Me-Nicotinyl)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

At page 146, delete Example 236 and insert:

Example 236

N-Ac-Sar-Gly-Val-D-Ile-Thr-Leu-Ile-Arg-ProNHCH₂(CH₃)₂

The procedure described in example 4 is used but substituting Fmoc-Leu for Fmoc-Nva.

After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-Ile-Thr-Leu-Ile-Arg-ProNHCH₂(CH₃)₂ as the trifluoroacetate salt.

At page 147, delete Example 240 and insert:

Example 240

N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Leu-Ile-Arg-ProNHCH₂(CH₃)₂CH₃

The procedure described in Example 206 is used but substituting Fmoc-Leu for Fmoc-Gln(Trt) and acylating with succinic anhydride after the coupling with Fmoc-Sar and deprotection as described in Example 54. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Leu-Ile-Arg-ProNHCH₂(CH₃)₂CH₃ as the trifluoroacetate salt.

At page 150, delete Example 249 and insert:

Example 249

The procedures described in Examples 49 is used but substituting the appropriate protected amino acids as described in Examples 14, 4, 75, 54 and 132 respectively. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-alloIle-Thr-Allygly-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Allygly-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Allygly-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-alloIle-Thr-Allygly-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Allygly-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-Ile-Ser-Allygly-Ile-Arg-Pro-ProNHCH₂CH₃, and
N-Ac-Sar-Gly-Val-D-Leu-Ser-Allygly-Ile-Arg-Pro-ProNHCH₂CH₃.

At pages 155-156, delete Examples 262-264 and insert:

Example 262

The procedures described in Example 46 is used but substituting the appropriate protected amino acids as describes in Examples 75, 4, 54, and 132. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-alloIle-Thr-Ala-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Ala-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Ala-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-alloIle-Thr-Ala-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Ala-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-Ile-Ser-Ala-Ile-Arg-ProNHCH₂CH₃, and
N-Ac-Sar-Gly-Val-D-Leu-Ser-Ala-Ile-Arg-ProNHCH₂CH₃.

Example 263

The procedures described in Example 262 is used but substituting Fmoc-Val for Fmoc-Ala. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-alloIle-Thr-Val-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Val-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Val-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-alloIle-Thr-Val -Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Val -Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-Ile-Ser-Val-Ile-Arg-ProNHCH₂CH₃, and
N-Ac-Sar-Gly-Val-D-Leu-Ser-Val-Ile-Arg-ProNHCH₂CH₃.

Example 264

The procedures described in Example 263 is used but substituting Fmoc-DNva for Fmoc-NvaVal. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA.

The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-alloIle-Thr-D-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-D-Nva -Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Val-D-Ile-Thr-D-Nva -Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-alloIle-Thr-D-Nva-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Ile-Thr-D-Nva -Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-Ile-Ser-D-Nva -Ile-Arg-Pro-ProNHCH₂CH₃, and
N-Ac-Sar-Gly-Val-D-Leu-Ser-D-Nva -Ile-Arg-Pro-ProNHCH₂CH₃.

At page 159-160, Examples delete 275-276 and insert:

Example 275

N-Ac-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₂CH₃

The procedure described in Example 13 is used but substituting Fmoc-D-Leu for Fmoc-D-Ile and Fmoc-Ser(tBu) for Fmoc-Thr(tBu). After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₂CH₃ as the trifluoroacetate salt.

Example 276

N-Ac-Sar-Gly-Val-D-Ile-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₂CH₃

The procedure described in Example 13 is used but substituting Fmoc-Ser(tBu) for Fmoc-Thr(tBu). After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-Ile-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₂CH₃ as the trifluoroacetate salt.

At page 161, delete Example 282 and insert:

Example 282

N-Ac-Sar-Gly-Val-D-alloIle-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₂CH₃

The procedure described in Example 276 is used but substituting Fmoc-D-alloIle for Fmoc-D-Ile. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield N-Ac-Sar-Gly-Val-D-alloIle-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₂CH₃ as the trifluoroacetate salt.

At pages 170-172, delete Examples 310-315 and insert:

Example 310

The procedure described in Examples 132 and 266 is used but substituting N-acetyl-6-aminocaproic acid (6-Ac-Aca) for acetic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(6-Ac-Aca)-Sar-Gly-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃, and

N-(6-Ac-Aca)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₃.

Example 311

The procedure described in Examples 310 is used but substituting N-acetyl-4-aminobutyric acid (4-Ac-Gaba) instead of N-acetyl-6-aminocaproic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(4-Ac-Gaba)-Sar-Gly-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃, and

N-(4-Ac-Gaba)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₃.

Example 312

The procedure described in Examples 311 is used but substituting 2-furoic acid instead of N-acetyl-4-aminobutyric acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(2-Furoyl)-Sar-Gly-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃, and

N-(2-Furoyl)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₃.

Example 313

The procedure described in Examples 311 312 is used but substituting shikimic acid instead of 2-furoic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(Shikimyl)-Sar-Gly-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃, and
N-(Shikimyl)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₃

Example 314

~~The procedure described in Examples 311 is substituting shikimic acid instead of 2-furoic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:~~

~~N-(Shikimyl)-Sar-Gly-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂(CH₃)₂, and~~
~~N-(Shikimyl)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂~~

Example 315

The procedure described in Examples 311 is used but substituting 2-methyl-nicotinic acid instead of 2-furoic acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(2-Me-nicotinyl)-Sar-Gly-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂(CH₃)₂CH₃, and
N-(2-Me-nicotinyl)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂CH₃

At pages 174-175, delete Example 323 and insert:

N-Ac-Sar-Gly-Val-D-Cys-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Gly-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val- D-Cys-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Succinyl-Sar-Gly-Val-D-Cys-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Ser-Nva-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-Cys-Ser-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Gly-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Ser-Ser-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Thr-Ser-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Thr-Leu-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Cys-Ser-Leu-Ile-Arg-ProNHCH₂CH₃,
N-Succinyl-Sar-Gly-Val-D-Cys-Ser-Ser-Ile-Arg-ProNHCH₂CH₃, and
N-Succinyl-Sar-Gly-Val-D-Cys-Ser-Leu-Ile-Arg-ProNHCH₂CH₃.

At page 177, delete Example 328 and insert:

Example 328

The procedures described in Example 326 is used but substituting the appropriate protected amino acids as describes in Examples 14, 15, 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Pen-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Pen-D-Leu-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Pen-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Pen-D-Ile-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Pen-D-Ile-Thr-Nva-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Pen-D-Ile-Thr-Nva-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Gly-Pen-D-Ile-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,

Example 323

The procedures described in Example 98 is used but substituting the appropriate protected amino acids as describes in Examples 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-Pen-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Gly-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Ser-Nva-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Succinyl-Sar-Gly-Val-D-Pen-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Ser-Nva-Ile-Arg-Pro-D-AlaNH₂,
N-Ac-Sar-Gly-Val-D-Pen-Ser-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Gly-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Ser-Ser-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Thr-Ser-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Thr-Leu-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen-Ser-Leu-Ile-Arg-ProNHCH₂CH₃,
N-Succinyl-Sar-Gly-Val-D-Pen-Ser-Ser-Ile-Arg-ProNHCH₂CH₃,
N-Succinyl-Sar-Gly-Val-D-Pen-Ser-Leu-Ile-Arg-ProNHCH₂CH₃, and
N-Succinyl-Sar-Gly-Val-D-Pen-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

At pages 175-176, delete Example 325 and insert:

Example 325

The procedures described in Example 324 is used but substituting the appropriate protected amino acids as describes in Examples 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Succinyl-Sar-Gly-Pen-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃, and
N-Succinyl-Sar-Gly-Pen-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

At pages 178-179, delete Examples 330-332 and insert:

Example 330

The procedures described in Example 329 is used but substituting the appropriate protected amino acids as describes in Examples 14, 15, 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-Ile-Pen-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-*allo*Ile-Pen-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Pen-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Pen-Ser-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Pen-Leu-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Pen-Nva-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Val-D-Ile-Pen-Nva-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Ile-Pen-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Succinyl-Sar-Gly-Val-D-Ile-Pen-Gln-Ile-Arg-ProNHCH₂CH₃, and
N-Succinyl-Sar-Gly-Val-D-Ile-Pen-Gln-Ile-Arg-ProNHCH₂(CH₃)₂.

Example 331

N-Ac-Sar-Gly-Val-D-Ile-Thr-Pen-Ile-Arg-ProNHCH₂CH₂OCH₃

The procedure described in Example 11 is used but substituting Fmoc-Pen(Trt) for Fmoc-Nva. After cleavage of the peptide from the resin and removal of the protecting groups the crude product was purified by C-18 column chromatography using solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions were lyophilized to yield N-Ac-Sar-Gly-Val-D-Ile-Thr-Pen-Ile-Arg- ProNHCH₂CH₂OCH₃ as the trifluoroacetate salt.

Example 332

The procedures described in Example 331 is used but substituting the appropriate protected amino acids as describes in Examples 14, 15, 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-alloIle-Thr-Pen-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Thr-Pen-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Pen-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Ile-Thr-Pen-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Pen-Ile-Arg-ProNHCH₂(CH₃)₂,
N-Ac-Sar-Gly-Val-D-Leu-Ser-Pen-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Gly-Pen-Ile-Arg-ProNHCH₂CH₃, and
N-Succinyl-Sar-Gly-Val-D-Leu-Ser-Pen-Ile-Arg-ProNHCH₂CH₃.

At page 180, delete Example 334 and insert:

Example 334

The procedures described in Example 333 is used but substituting the appropriate protected amino acids as describes in Examples 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Gly-Val-D-Phe(3,4,5-triF)-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Phe(3,4,5-triF)-Gly-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Phe(3,4,5-triF)-Ser-Leu-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Phe(3,4,5-triF)-Ser-Nva-Ile-Arg-Pro-D-AlaNH₂,
N-Succinyl-Sar-Gly-Val-D-Phe(3,4,5-triF)-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,

N-Succinyl-Sar-Gly-Val-D-Phe(3,4,5-triF)-Ser-Gln-Ile-Arg-ProNHCH₂CH₃,

N-Succinyl-Sar-Gly-Val-D-Phe(3,4,5-triF)-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂,

N-Ac-Sar-Gly-Val-D-Phe(3,4,5-triF)-Ser-Gln-Ile-Arg-ProNHCH₂CH₃, and

N-Ac-Sar-Gly-Val-D-Phe(3,4,5-triF)-Ser-Ser-Ile-Arg-ProNHCH₂CH₃.

At pages 181-182, delete Example 336 and 337 and insert:

Example 336

The procedures described in Example 335 is used but substituting the appropriate protected amino acids as described in Examples 132, 43, 54, and 75. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-Ac-Sar-Ala-Val-D-Leu-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,

N-Ac-Sar-Ala-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,

N-Ac-Sar-Ala-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,

N-Ac-Sar-Ala-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂CH₃,

N-Succinyl-Sar-Ala-Val-D-Ile-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,

N-Succinyl-Sar-Ala-Val-D-Ile-Thr-Gln-Nva-Ile-Arg-ProNHCH₂CH₃,

N-Succinyl-Sar-Ala-Val-D-Ile-Thr-Gln-Nva-Ile-Arg-ProNHCH₂(CH₃)₂, and

N-Succinyl-Sar-Ala-Val-D-Ile-Thr-Gln-Nva-Ile-Arg-Pro-D-AlaNH₂.

Example 337

The procedure described in Example 231 used but substituting N-acetyl-beta-alanine (3-Ac-Bala) for N-acetyl-4-aminobutyric acid. After cleavage of the peptide from the resin and removal of the protecting groups using (9:1) TFA/anisole (3 mL) the crude product is purified by C-18 column chromatography using a solvent mixture varying in a gradient of 10% to 50% acetonitrile-water containing 0.01% TFA. The pure fractions are lyophilized to yield the following peptides as trifluoroacetate salt:

N-(3-Ac-Bala)-Sar-Gly-Val-D-alloIle-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,

N-(3-Ac-Bala)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,

N-(3-Ac-Bala)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-Pro-D-AlaNH₂,
N-(3-Ac-Bala)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-Pro-DAlaNH₂,
N-(3-Ac-Bala)-Sar-Gly-Val-D-alloIle-Thr-Gln-Ile-Arg-ProNHCH₂(CH₃)₂,
N-(3-Ac-Bala)-Sar-Gly-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Gly-Val-D-Leu-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Gly-Val-D-Pen-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Gly-Val-D-Ile-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Ala-Val-D-alloIle-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Ala-Val-D-Ile-Ser-Nva-Ile-Arg-ProNHCH₂CH₃,
N-(3-Ac-Bala)-Sar-Ala-Val-D-Leu-Ser-Nva-Ile-Arg-ProNHCH₂CH₃, and
N-(3-Ac-Bala)-Sar-Ala-Val-D-Leu-Ser-Gln-Ile-Arg-ProNHCH₂CH₃.